

The University of Chicago

THE MOLECULAR REARRANGE-
MENT OF 2-DIMETHYLAMINO-
TETRAMETHYLETHANOL
HYDROCHLORIDE

A DISSERTATION SUBMITTED TO THE FACULTY OF THE
DIVISION OF THE PHYSICAL SCIENCES IN CANDIDACY
FOR THE DEGREE OF DOCTOR OF PHILOSOPHY

DEPARTMENT OF CHEMISTRY

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VAN VERNON ALDERMAN

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Introduction

A molecular rearrangement may be defined as an irreversible reaction which produces a change in the structural grouping of the molecule undergoing rearrangement and with which may be associated an elimination of such simple molecules as water, nitrogen, or hydrogen halide. Thus the conversion of N-halogen acid amides to primary amines, of triphenylmethylhalogen amines to phenylimidobenzophenone, and of certain glycols and amino-alcohols to aldehydes and ketones are molecular rearrangements. Consideration of the mechanism by which such new orientation of atoms or radicals within a molecule takes place serves to correlate existing data, predict related phenomena and demonstrate the nature of and the effect of the environment on the bonding forces of atoms within molecules.¹

Dr. Stieglitz and a number of his students have sought, by a study of the general properties of pinacols and the closely related alkamines, a firm basis on which to postulate the mechanism of their rearrangement. The recent use of this rearrangement as a technique for comparing migrational tendencies of different groups and thereby deriving data revelatory of affinity distribution within molecules,^{2, 3, 4} while of interest, is not directly related to this older problem. We present here an exposition of the Stieglitz theory of the pinacol rearrangement and of the evidence that has been brought to support it, including our work on 2-dimethylaminotetramethylethanol hydrochloride.

¹Stieglitz, Proc. Nat. Acad. Sci., 1, 196-202 (1915).

²"Ann. Repts. Chem. Soc.," London, 1930, Vol. XXVII, p. 114.

³Bachmann and Sternberger, J. Am. Chem. Soc., 56, 170 (1934).

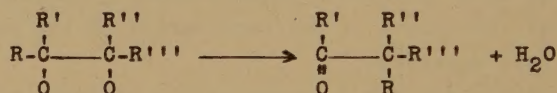
⁴Tiffeneau, Bull. soc. chim., 49, 1903 (1931).

A. The Pinacol-Alkamine Rearrangement

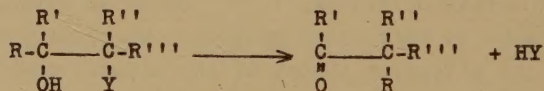
1. Historical Review

Certain classes of molecular rearrangements such as the pinacol, semi-pinacol, semi-hydrobenzoin, halohydrin, and alkamine are closely related.⁵ That this resemblance is not merely one of structural similarity, i.e., the presence of two adjacent carbon atoms to which are attached strongly electronegative groups (hydroxyl, amino, and halogen), is shown by the common rearrangement of these molecules to carbonyl compounds, and their similar behavior toward common rearranging agents.

The general equation,



in which R, R', R'', R''' may be hydrogen atoms, alkyl or aryl groups, alike or unlike, symmetrically arranged or not, or even components of a cyclic structure built about a part or the whole of the ethane nucleus,⁶ may be extended to the still more general equation,



⁵For comprehensive reviews of the subject see the following sources: K. H. Adams, "Molecular Rearrangement of Pinacol Derivatives," Ph.D. dissertation, Department of Chemistry, University of Chicago, 1932; "Ann. Repts. Chem. Soc.," London, 1933, Vol. XXX, p. 183; Porter, "Molecular Rearrangements," Chemical Catalogue Co., New York, 1928; E. S. Wallis, "Molecular Rearrangements" in "Organic Chemistry, An Advanced Treatise," ed. Henry Gilman, John Wiley & Sons, New York, 1938, Vol. I, p. 720.

⁶For example, diethyltetramethyleneglycol rearranges under the influence of acid to two ketones, 2,2-diethylcyclohexanone and 1,1-ethylpropionylcyclopentane respectively. Meerwein, *Ann.*, 393, 200 (1913). Contraction or expansion of the ring may result, or the ring itself may not be affected.

where Y represents halogen, amino,⁷ hydroxyl,⁸ probably thiol, and in general any simple group of which the hetero atom is electronegative or strongly electron attracting as compared to the attached carbon atom.

The groups, OH and Y, should, generally speaking, be substituted on adjacent carbon atoms. Thus, 2-hydroxy-2,2-diphenyl-1-benzylethylamine may be rearranged with nitrous acid; 3-hydroxy-1,3,3-triphenylpropylamine which has the methylene group between the two carbon atoms holding the functional groups cannot be.⁹ Though a few 1-3 glycols give carbonyl compounds, usually 1-4 glycols form furane derivatives.^{10, 11} Those compounds in which the functional groups are more than two and situated on adjacent carbon atoms may rearrange. Acrolein is, conceivably, a product of the rearrangement of glycerine. But to avoid confusion, the definition of the pinacol type of rearrangement is limited to that for which the above general equation was drawn.

When the groups R are different or unsymmetrically located on the ethane nucleus, more than one ketone may result on rearrangement. Among the related factors that decide which functional group be lost and ketone produced are the relative strengths of the carbon-hetero atom bonds determined by the radicals R¹² and the electronegative character of Y, and the sensitivity of either functional group toward attack by a specific reagent.

Alkamines and the corresponding glycols do not necessarily rearrange to the same product. The alkamine, 2-amino-3,3-diphenyl-

⁷McKenzie and Roger, J. Chem. Soc., 571 (1927).

⁸"Ann. Repts. Chem. Soc.," London, 1930, Vol. XXVII, p. 114.

⁹McKenzie, J. Chem. Soc., 123, 89 (1923).

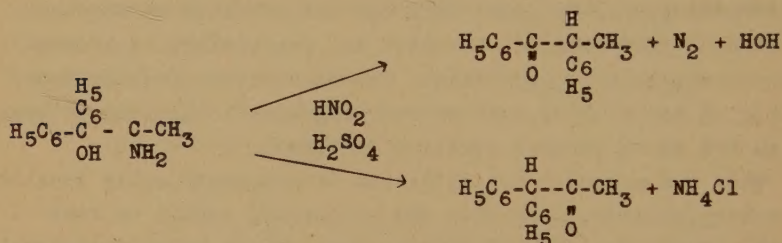
¹⁰Beilstein, "Handbuch der Organischen Chemie," Julius Springer, Berlin, 1918, Vol. I, pp. 481-99; supplement to Vol. I, pp. 250-65.

¹¹Shepard and Johnson, J. Am. Chem. Soc., 54, 4385 (1932).

¹²Thus Bachmann finds that in the symmetrical pinacols the anisyl groups migrate less readily than the phenyl groups. J. Am. Chem. Soc., 55, 3819 (1933). In the unsymmetrical pinacols, however, the reverse appears to be the case. Migita ascribes this anomalous behavior as being due to the weakening of the carbon hydroxyl bond by the more electronegative phenyl group. Once the hydroxyl group is lost, the anisyl group must wander. Migita, Bull. Chem. Soc. Japan, 8, 22 (1933).

propanol-3 yields 1,2-diphenylpropanone-1;¹³ the corresponding glycol, 3,3-diphenylpropanone-2;¹⁴ and the oxide produced as a by-product in the deamination of the alkamine, the ketone obtained from the glycol. Any directional influence exerted by the wholly similar groups in each of the molecules was rendered impotent by the specificity of the nitrous acid reagent toward removing the amino group.

Certain unsymmetrical aminoalcohols treated with nitrous acid at low temperatures give the normal ketone by migration of a group to the carbon atom holding the amino group, and another ketone when rearranged by acids at higher temperatures.¹⁵



The higher the temperature and the greater the excess of acid the more rearrangement is apt to occur through loss of the hydroxyl group.¹⁶

The glycol, 1-phenyl-2-ethylbutanediol-1,2 heated with hot dilute sulphuric acid yields phenyldiethylacetaldehyde; with cold concentrated sulphuric acid, 3-phenylhexanone-4; and with phosphorus pentoxide, diethylstyrolene.¹⁷ Similar results have been obtained with other glycols.¹⁸

¹³McKenzie, Roger, Wills, J. Chem. Soc., 779 (1926); McKenzie and Myles, Ber., 65B, 209 (1932).

¹⁴Stoemer et al., Ber., 39, 2288 (1906).

¹⁵Bettzieche, Z. Physiol. Chem., 140, 140 (1924); 140, 261 (1924). For other examples, see: Orekhov and Robers, Compt. rend., 180, 70 (1925); P. Brauer, "The Molecular Rearrangement of 2-phenylaminotetramethylethanol," Ph.D. dissertation, Department of Chemistry, University of Chicago, 1933.

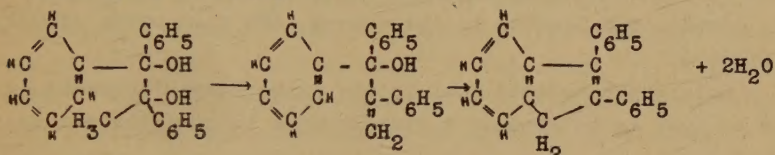
¹⁶Ehman, Ph.D. dissertation, Department of Chemistry, University of Chicago, 1935.

¹⁷Tiffeneau and Levy, Bull. soc. chim., 33, 735 (1923).

¹⁸Orekhov and Tiffeneau, ibid., 23, 211 (1918).

The common rearranging agent for alkamines has been nitrous acid; for glycols, sulphuric acid and such agents as acetyl chloride; for halohydrins, silver and mercury salts and heat alone.¹⁹ Pinacol has been converted to pinacolone by treatment at 300°-320° with alumina.²⁰ Undoubtedly this pyrolysis technique could be extended to the rearrangement of other glycols.

Dehydration, dehydrohalogenation, or deamination of these substituted ethanols may produce organic cyclic oxides and vinyl derivatives as well as products of rearrangement. Dimethylbutadiene has been obtained by distillation of pinacol from concentrated sulphuric acid.²¹ Numerous instances of vinyl type dehydration exist in the literature of which the following is particularly interesting:²²



Dilute acids, furthermore, which certainly possess no specific deamination and dehydration abilities, cause the rearrangement of both alkamines and glycols. At 100° pinacol rearranges at a rate directly proportional to the hydrogen ion concentration; sulphuric and phosphoric acids rearrange pinacol more slowly than does hydrochloric acid.²³ Water at 200°-210° converts it to pinacolone; anhydrous pinacol heated alone at this temperature undergoes no change.²⁴ The rate of rearrangement of several alkamines is that of a pseudomonomolecular reaction.

Any mechanism, therefore, that is offered for this re-

¹⁹Ayers, J. Am. Chem. Soc., 60, 2957 (1938), also Tiffeneau, Compt. rend., 145, 593 (1907).

²⁰Patiev, J. Russ. Phys. Chem. Soc., **38**, 1, 92 (1906);
Abs. J. Chem. Soc., 1907, I, 6.

²¹Bayer and Co., Chem. Zentr., 1912, II, 1757.

²²O. Blum Bergman, Abs. J. Chem. Soc., 1932, 273. For further illustrations, see "Ann. Repts. Chem. Soc.," London, 1933, Vol. XXX, p. 183.

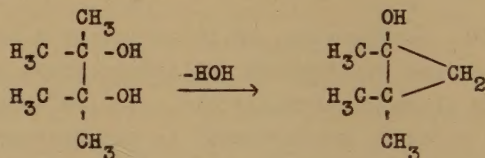
²³Stieglitz, Cooper and Ayers, Trans. Ill. State Acad. Sci., 25, 173 (1933).

²⁴Adams, op. cit.

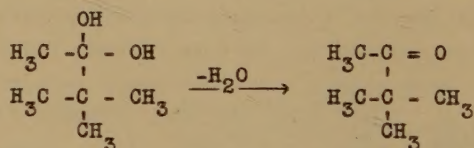
arrangement must (1) take into account its general nature which connotes a variety of R and Y substituents, (2) explain qualitatively the factors which control the relative stabilities of the functional group, and (3) account for the fact that rearrangement neither follows dehydration or deamination always, nor is necessarily produced by dehydrants and deaminants.

Those mechanisms offered for the rearrangement of pinacol and related derivatives since the early discovery of Fittig that concentrated sulphuric acid converted tetramethylethylene glycol into methyletert-butyl ketone or pinacolone,²⁵ postulate either a known type of compound or a highly unstable and transitory free radical as the intermediate through which the rearrangement progresses. In the first class may be grouped the theories of Erlenmeyer, Breuer, and Zincke; in the second, the open oxide structure of Tiffeneau.

Erlenmeyer assumed that in the pinacol rearrangement water is so lost as to produce a cyclopropane as an intermediate,



which adds a molecule of water to give a 2,2-dihydroxybutane, spontaneously (two hydroxyl groups on the same carbon atom) dehydrating to pinacolone.²⁶



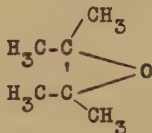
On the basis of this theory a pinacol such as tetra-(p-chlorophenyl)-ethylene glycol should rearrange to a compound having a phenyl group substituted in its meta position with chlorine. But Montagne showed that the chlorine groups are still substituted in

²⁵Fittig, Ann., 110, 25 (1859); 114, 54 (1860).

²⁶Erlenmeyer, Ber., 14, 322 (1881).

the para position in all the phenyl groups of the ketone.²⁷ A similar experiment was performed by Acree using methyl groups as "tags" rather than chlorine atoms.²⁸

Breuer and Zincke also postulated a dehydration which involved both hydroxyl groups of the glycol to form a derivative of ethylene oxide.²⁹



The corresponding oxides of certain pinacols rearrange (tetramethylethylene oxide yields pinacolone when distilled under atmospheric pressure;³⁰ sym. 1,2-diphenyl-1,2-dimethylethylene oxide at 200°-300°, a ketone also³¹), and often,^{32, 33} but not always,³⁴ the rearrangement products of the pinacols and their oxides are identical. To convert an oxide into an aldehyde or ketone is usually more difficult than to change the glycol into the same product.³⁵ Meerburg showed that the rate of rearrangement of the oxide of 4,4',4'',4''' tetrachlorbenzpinacol was slower than that of the glycol.³⁶ Alkamines and their correspond-

²⁷Montagne, Rec. trav. chim., 24, 105 (1905); 25, 413 (1906).

²⁸Acree, Am. Chem. J., 33, 180 (1905).

²⁹Breuer and Zincke, Ber., 11, 68 (1878); 16, 400 (1882).

³⁰Delacre, Bull. soc. chim., 147, 1, 586 (1907).

³¹Mme. Ramart Lucas and Legagneur, Compt. rend., 188, 1848 (1929).

³²Delacre, loc. cit.

³³Tiffeneau, Orekov, Levy, Compt. rend., 179, 977 (1924).

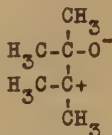
³⁴Adams, op. cit.; "Ann. Repts. Chem. Soc.," London, 1933, Vol. XXX, p. 183; Porter, op. cit.; Wallis, loc. cit.

³⁵Porter, op. cit., p. 91; Klages, Ber., 38, 1970 (1905); Tiffeneau, Bull. soc. chim., 29, 809 (1921); see also Adams, op. cit.

³⁶Meerburg, Rec. trav. chim., 24, 105 (1905); 28, 272 (1909).

ing glycols do not necessarily yield the same ketones.^{37, 38} From these and similar results the theory of Breuer and Zincke has fallen into disrepute.

The free radical theory of Tiffeneau claims a compound possessing the open oxide type of structure as the intermediate in the pinacol rearrangement.³⁹



Though here are implicit the more modern electronic theories, in that a positive carbon atom (possessing only a sextet of electrons) is postulated and in that the wandering of a negative group rectifies this unsaturation, the theory accounts for neither the achievement of dehydration with dilute acids, nor the maintenance of optical activity in certain of the pinacols during the course of rearrangement. That free radicals can possess a transient existence without loss of optical activity seems to be contrary to recorded experience.⁴⁰

We have ignored in this brief review the theories of Faworsky (dioxane type intermediate produced by an intermolecular reaction between pinacol molecules), of Michael,⁴¹ of Lachman who claims a simultaneous interchange between the methyl and hydroxyl group of pinacol to produce the 2,2-dihydroxybutane⁴² noted in Erlenmeyer's theory.

These mechanisms without exception have failed in one way or another to satisfy a broad interpretation of the pinacol-

³⁷ McKenzie, Roger, Wills, loc. cit.; McKenzie and Myles, loc. cit.

³⁸ Stoemer et al., loc. cit.

³⁹ Tiffeneau, Compt. rend., 143, 684 (1906); Ann. chim.(8), 10, 322 (1907); Bull. soc. chim.(4), 1, 1221 (1907); 49, 1595 (1931); Meerwein, Ann., 396, 200 (1931); 419, 121 (1919).

⁴⁰ Gilman, op. cit., p. 770.

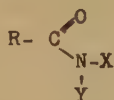
⁴¹ For a review of these theories, see Porter, op. cit., pp. 92-95; also, Gilman, op. cit., p. 749.

⁴² Gilman, ibid., p. 767.

alkamine rearrangement. It is believed that the theory presented in the following pages avoids these difficulties.

2. The Electron Theory of Molecular Rearrangement

The early speculations of Dr. Stieglitz regarding the Lossen-Beckman, Curtius, and Hofman rearrangements of acylhydroxylamines and ketoximes, acylazides and acylhalogenamines led him to extend the work on these derivatives to the analogous triphenylmethyl hydroxylamines, halogenamines, and azides.⁴³ The mechanism, advanced for these rearrangements, applicable in its broader aspects to the pinacol and alkamine rearrangements, states that in the molecule,



(where XY independent of N represents a molecule of hydrogen halide, water, or the two atoms of the azide group), the contributing cause toward rearrangement is the capture of electrons from the nitrogen atom by the removal of a molecule of hydrogen halide, water, or nitrogen effected by the appropriate reagent.⁴⁴ The instability of the nitrogen atom left with a sextet of electrons where normal stability demands an octet induces in the interatomic forces of the residue a strain which is adjusted by the movement of radical R (with its complement of electrons) to the nitrogen atom; redirection of the forces within the fragment leads to an isocyanate, the recognized intermediate in the rearrangement.

The "fault" in the molecule lay in the positiveness of the group Y. "The labile component in the original molecule is an unstable positive radical or atom, which tends to go over into the stable negative form."^{45, 46}

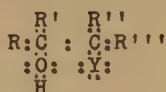
⁴³For a general bibliography of Dr. Stieglitz's work, see McCoy, "Julius Stieglitz," J. Am. Chem. Soc., **60**, 19 (Nov., 1938).

⁴⁴Stieglitz, Am. Chem. J., **15**, 215, 504 (1893); **18**, 751 (1896).

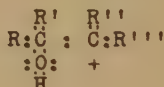
⁴⁵Stieglitz, J. Am. Chem. Soc., **44**, 1293 (1922); Proc. Nat. Acad. Sci., **1**, 196 (1915).

⁴⁶For a review of the modern electronic theory of valence as applied to organic compounds, see John R. Johnson, "Modern

In the 1-2 glycol, alkamine, and halohydrin species of molecule,



exist two similar sources of instability: the adjacent partially oxidized carbon atoms which may through intramolecular oxidation-reduction give rise to molecular rearrangement,⁴⁷ and the grouping $\text{:}\ddot{\text{C}}:\ddot{\text{Y}}:$ which consists of an electronegative atom and an atom neither strikingly electronegative nor positive,⁴⁸ with the electron pair uniting the two atoms displaced toward Y. Neither of these conditions is sufficient to produce the actual rearrangement, though both create the necessary instability within the molecule which must be the prelude to rearrangement. The reagent that loosens the bond :C:Y: ruptures the two atoms in such a way that Y acquires a doublet of electrons at the expense of C, and the residue



must adjust itself in one or more of three ways.⁴⁹

1) The fragment may absorb a negative group from the environment. That this can take place is evidenced by the discovery of Ayers that the decomposition of the hydrogen bromide salt of pinacol under anhydrous conditions yields tetramethylethylene-bromohydrin.⁵⁰ The dry hydrogen bromide salt of tert-butylcarbinol, stable at 45°, decomposes at 65° into a mixture of bro-

Electronic Concepts of Valence," in Gilman, *op. cit.*, Vol. II, p. 1595.

⁴⁷Jones, *Am. Chem. J.*, **50**, 414 (1913).

⁴⁸The generalized system $\text{:}\ddot{\text{A}}:\ddot{\text{B}}:\ddot{\text{Y}}:$ in which the components are defined as in the text has been brought forward in the literature. (Whitmore, *J. Am. Chem. Soc.*, **54**, 3274 [1932].) With loss of $\text{:}\ddot{\text{Y}}:$, the fragment $\text{:}\ddot{\text{A}}:\ddot{\text{B}}$ may adjust itself in one of three ways:

- 1) assumption of X- from solution
- 2) loss of a proton and production of vinyl derivative
- 3) molecular rearrangement.

⁴⁹See preceding footnote.

⁵⁰Stieglitz, Cooper and Ayers, *loc. cit.*

mides of which 72 per cent was identified as tert-amylbromide.⁵¹ Nitrous acid acting upon certain alkamines gives small yields of the corresponding glycols along with the normal rearrangement products.⁵²

2) The fragment may lose a proton to produce an oxide or a vinyl derivative. Dimethylbutadiene has been obtained from pinacol. When a monohydric tertiary alcohol is dehydrated a structural modification, known as the Wagner rearrangement, occurs which gives an olefinic derivative. Thus, diphenyltert-butylcarbinol may be converted into 3,3-diphenyl-2-methylbutene-1.⁵³ Presence of an olefine or an oxide in the rearrangement products therefore provides no proof of the validity of the older theories. The formation of an oxide indicates that a "free" electron pair of the hydroxyl group became attached to the positive carbon atom and the proton of the group was abandoned. The resulting oxide happened to be stable to the environment.

3) The fragment may rearrange. An atom is most stable when in a completely reduced or in a completely oxidized state. By the wandering of a group R to the positive carbon atom intramolecular oxidation-reduction is achieved. That group wanders which has most complete control of the doublet uniting it to the carbon atom. A "free" electron doublet on the hydroxyl oxygen is immediately taken by this now unsaturated carbon atom; the proton, freed, and rearrangement is complete.

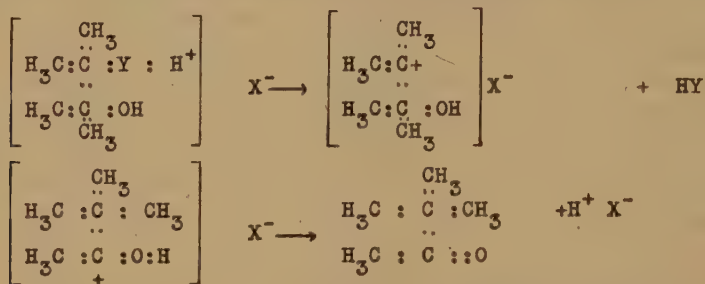
All reagents must, if this theory is correct, have but one effect, the production of the unsaturated ethanol fragment through dehydration or dehalogenation or deamination. Since the bond $\text{:}\ddot{\text{C}}\text{:}\ddot{\text{Y}}\text{:}$ must be ruptured before rearrangement occurs and acids do effect rearrangement, this bond must be attacked by acid. This attack, according to the Stieglitz theory, probably lies in the formation of an "onium" salt of $\text{:}\ddot{\text{Y}}\text{:}$ which must necessarily have that unshared pair of electrons needed for salt formation. The existence of ammonium salts is beyond dispute; the existence of oxonium salts, even under conditions that are not anhydrous, has

⁵¹Whitmore and Rothrock, J. Am. Chem. Soc., **54**, 3431 (1932).

⁵²McKenzie, J. Chem. Soc., **123**, 89 (1923).

⁵³Batemen and Marvel, J. Am. Chem. Soc., **49**, 2914 (1927).

been accepted.⁵⁴ In the free base the unshared electron doublet is believed to contribute to the strength of the carbon-hetero atom bond by giving the carbon atom, positive from the polar standpoint, something else "to cling to." This so-called electro-
meric effect⁵⁵ is neutralized by the addition of a proton, and the carbon-hetero atom bond correspondingly weakened. Rearrange-
ment takes place by the breaking off of the saturated molecule $H:\ddot{Y}:$, and a reorientation of atoms within the residue:



The existence of the above intermediate fragment as a positively charged radical has been seriously questioned by a number of investigators. Both 3-phenyl-2-benzyl-1-naphthylpropanediol-1,2⁵⁶ and 1,3-diphenyl-2-benzylpropanediol-1,2⁵⁷ have been rearranged. Cold sulphuric acid in each case gives a racemic ketone; hot dilute sulphuric acid, an optically active product consisting of both racemic and optically active ketones.⁵⁸ This maintenance of optical activity does not seem to be a general rule. In view of these results and those of Wallis and Adams indicating the optical instability of carbonium ions,⁵⁹ satisfactory mechanisms may demand that the migrating group be never wholly

⁵⁴Kehrmann, "Oxonium Verbindungen," in "Die Methoden der Organischen Chemie," Houben, George Thieme, Leipzig, 1930, Vol. III, p. 317. See also the works of Ayers.

⁵⁵See John R. Johnson, op. cit.; Gilman, op. cit., Vol. II, p. 595.

⁵⁶McKenzie and Dennler, Ber., 60B, 220 (1927).

⁵⁷Roger and McKenzie, Ber., 62B, 272 (1929).

⁵⁸McKenzie, Roger, Wills, loc. cit.; McKenzie and Myles, loc. cit.

⁵⁹Wallis and Adams, J. Am. Chem. Soc., 55, 3838 (1933); Wallis and Bowman, J. Org. Chem., 1, 383 (1936).

free and under the influence of the electron deficient carbon atom in such a way that the asymmetry of that atom remains unchanged, or that the loss of the functional group and migration of the radical occur simultaneously. Jones and Wallis were led to the former view after their discovery that optical activity was maintained throughout the rearrangement of d-benzylmethylacetazide.⁶⁰ Bartlett supports the latter view with his studies on the rearrangement of the geometrical isomers of 1,2-dimethylcyclohexanediol-1,2 and of 1,2-dimethylcyclopentenediol-1,2.⁶¹ Only in the cis form of either glycol did the methyl group migrate in preference to the ring carbon atom indicating that migration of a group cannot occur unless it reach the "face" opposite to the hydroxyl group which it replaces. With the trans form of the cyclohexane glycol, ring contraction occurred; with that of the cyclopentane glycol, polymers were obtained indicating diene formation. While these complementary views must be extended to the general pinacol rearrangement with caution because of their derivation from what may be special cases and their vagueness as to the valency forces acting, they do present strong reason to doubt the existence of the carbonium ion as an intermediate, however unstable and transitory.

The actual path for rearrangement through the "onium" compound, however, should be capable of experimental demonstration. If P represent the glycol or amino alcohol, PH⁺ rearranges. Since the formation of the salt and the rearrangement of the unsaturated fragment must be very fast, dehydration or deamination should be the rate controlling reaction. Therefore among the factors controlling the rate of rearrangement such as temperature and the stability of the carbon-hetero atom bond we may include the concentration of PH⁺. For the salt of any one molecular species of weak basicity with a strong acid, at any one temperature, and in dilute solution, the actual rate of rearrangement should be a linear function of the concentration of acid.

Cooper demonstrated clearly that the rate of rearrangement of pinacol followed linearly the concentration of acid, and that the data could be fitted, within the precision of measure-

⁶⁰Jones and Wallis, J. Am. Chem. Soc., 48, 169 (1926). See also Gilman, loc. cit.

⁶¹Bartlett and Pockel, J. Am. Chem. Soc., 59, 820 (1937); 60, 2416 (1938).

ment, to the equation for a pseudo unimolecular reaction. This work indicated the probable truth of the assumption made in the theory.

Since it was desirable to study the salt PHX of some stronger base with a strong acid, the rate of rearrangement of 2-aminotetramethylethanol was studied by Dr. Adams over a wide range of acid concentration at 175°. The theory as stated anticipated that up to complete salt formation (equivalency of acid with amine) the rate of rearrangement is a linear function of the acid concentration; and predicted that beyond equivalency the rate should not be further affected by acid. Dr. Adams found, however, that excess of acid accelerated markedly the rearrangement of the alkamine; from this he concluded that the measured rate of rearrangement represented the rate of two concurrent reactions, those of deamination and dehydration respectively. Rearrangement through the oxonium salt occurs particularly at high concentrations of free acid and at high temperatures. Further uncertainty in the interpretation of the data (derived from the rearrangement of this alkamine and other derivatives in this series) is afforded by our lack of precise knowledge concerning the activities of the involved ions at the high temperatures and in the moderately concentrated solutions used.

The alkamine, 2-phenylaminotetramethylethanol, being a weaker base than the 2-amino compound, should form a salt more highly hydrolyzed and more sensitive to excess of acid. But since the phenylamino-carbon bond is weaker than the amino-carbon bond and a lower temperature is required for rearrangement, less rearrangement should take place through the hydroxyl group. Actually where Adams found a tenfold increase in acid accelerated the rearrangement of 2-aminotetramethylethanol hydrochloride eight- to tenfold, Brauer found a comparable increase of acid affected the rearrangement only by a factor of 1.2.

The rate of rearrangement of 2-dimethylaminotetramethylethanol hydrochloride was studied over a limited range of acid concentration and at two temperatures. While this compound could not be expected to rearrange at a significantly lower temperature than the 2-amino derivative, a study of its rearrangement should be:

1) a corroboration in essential respects of Dr. Adams' results;

2) a further check on the general validity of the theory;

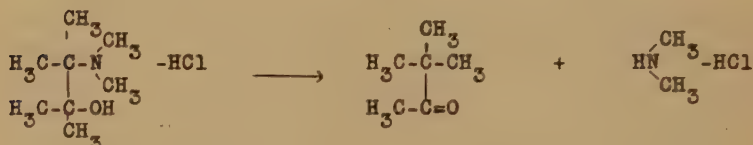
3) concerned with a alkamine whose tertiary nitrogen atom held no labile hydrogen atom and therefore could not be expected to undergo a simple dehydration to arrive at the positive carbon radical postulated by Tiffeneau.

B. Discussion of Results

1. Introduction

The alkamine, 2-dimethylaminotetramethylethanol hydrochloride, was prepared in 42 per cent yield by the interreaction of tetramethylethylenedichlorohydrin and aqueous dimethylamine at 100°. The preparation of this compound and other derivatives is described in the experimental part.

The fact that the equation



accurately expresses the rearrangement of this alkamine was demonstrated (1) by the isolation of 93 per cent of the theoretically obtainable pinacolone as its 2,4-dinitrophenylhydrazone, and (2) by the precision with which the points (Time - log.C) in the rate studies, over a wide range of acid concentration, followed the straight line indicative of a first order reaction. Pinacolone was determined by means of its 2,4-dinitrophenylhydrazone.

Polymer formed during the course of rearrangement was negligible in most of the runs; only in the aqueous solution of the salt heated at 175° for over twenty hours was sufficient polymer obtained to depress appreciably the melting point of the 2,4-dinitrophenylhydrazone and make aberrant the rate curve. The tendency of K (calculated on the long interval basis) to assume progressively lower values as the rearrangement proceeded was most exaggerated in the runs of lowest acid concentration, and in those runs in which the polymer was most manifest. That side reactions were not more prominent, and that this investigation could be carried out over 80 per cent of the reaction range with considerable certainty are of interest.⁶²

⁶²Gilman, op. cit., I, 838.

2. Method of Analyses

a. Estimation of dimethylamine or the ethanolamine.--While either of these amines could be determined precisely by a modification of the technique used in the Kjedahl analysis for the estimation of ammonia, simple distillation technique would not effect in aqueous solution their separation. Attempts to free the alkamine (b.p.= 180°) from the much more volatile dimethylamine (b.p.= 7°) by blowing of nitrogen through an alkalinized solution of the two were likewise ineffectual.

Experiments designed to eliminate the secondary amine through formation of its neutral nitroso derivative disclosed that conditions conducive to 100 per cent nitrosamine formation destroyed approximately 40 per cent of the amino alcohol. Whether the action of the nitrous acid was one of rearranging or oxidative scission of the alcohol was not determined. The above quoted figure means 40 per cent of the basicity, whether from alkamine, a tertiary amine or dimethylamine, was lost from the system. An obvious accounting for this is in the formation of nitrogen or a nitroso derivative. But no pressure was observed in the Carius tubes in which the reaction was carried out, nor was pinacolone isolable.

b. Estimation of pinacolone.--As most methods of analysis for ketones promised to be unsuitable because of their reliance upon anhydrous conditions or their lack of dependability under all save the most rigorously defined environments,⁶³ study was made of the precipitation of the 2,4-dinitrophenylhydrazone of pinacolone from an acidulated aqueous methanol solution of the ketone whose concentrations ranged from 0.1 M. to 0.02 M. in the presence of both dimethylamine and 2-dimethylaminotetramethylethanol hydrochlorides. It was found (Table 11) that from a solution 50 per cent water, 43 per cent methanol, 1.2 M. with respect to sulphuric acid, and of 40 cc. volume, pinacolone can be recovered as its 2,4-dinitrophenylhydrazone to the extent of 97.5 ± 0.5 per cent. In concentrations of pinacolone above 0.04 M. the precision is ± 0.2 per cent. Macro gravimetric technique was used throughout, and any small errors implicit in the handling and weighing of a

⁶³For a review of methods, see Adams, *op. cit.*; also S. Gershon, M.S. dissertation, Department of Chemistry, University of Chicago, 1935. See also, Bryant and Smith, *J. Am. Chem. Soc.*, 57, 57 (1935).

precipitate are proportionally magnified, the smaller the precipitate.

A short study was made of the variables, concentration of acid, of methanol and of water, and volume of the precipitating solution, before there was achieved the balance of these necessary to give a consistent 97 per cent yield of isolable hydrazone. These variables are discussed briefly in the following paragraphs:

1. Volume of precipitating solution.--(Table 10.) Out of a solution of 30 cc. 95.4 per cent of the pinacolone was recovered as its hydrazone, opposed to a recovery of 93.9 per cent from a solution of 40 cc. This difference lies outside experimental error and may be accounted for by the solubility of the hydrazone in a 34 per cent aqueous methanol solution, 1.6 M. with respect to sulphuric acid.

2. Concentration of acid.--(Table 9.) In this set of experiments the concentration of water was held at 25 per cent, the methanol at 65 per cent while the concentration of sulphuric acid was varied from 1.2 M. to 1.6 M. to 2.2 M. While increase of the acid concentration from 1.2 M. to 1.6 M. dropped the percentage of pinacolone recovered only slightly (90.2 per cent to 89.9 per cent), further increase of acid to 2.2 M. reduced the percentage recovered to 86.6 per cent. Apparently this higher concentration of acid serves to hydrolyze the hydrazone formed, or actually to hinder its formation.

The maximum concentration of hydrochloric acid used in any rearrangement study was 2.08 N. Addition of 10 cc. of acid of this normality to the precipitation solution (vol. = 40 cc.) would render the solution ($\text{H}_2\text{SO}_4 = 2.4 \text{ N.}$). This is still well within tolerance.

3. Concentration of water in methanol.--(Tables 7, 8.) The water percentage was varied from 25 to 56 per cent (entailing a corresponding change in methanol of 37 per cent to 68 per cent), and this produced a gradual increase of pinacolone recovered from 90.2 per cent to 97 per cent. The high percentage of water could not be present in the solution at the time of the addition of the reagent since it caused precipitation of the latter. Therefore the hydrazine and the ketone were mixed in a solution approximately 25 per cent with respect to water; and shortly before filtration sufficient water added to make the solution 56 per cent aqueous. Increase in the concentration of water beyond 50 per cent did not exert an appreciable effect on the amount of hydrazone precipitated.

Various blank runs made by adding the hydrazine reagent to strongly acidulated solutions of 2-aminotetramethylethanol hydrochloride and of its dimethyl derivative, and also by precipitating the hydrazone of pinacolone in the presence of the amine hydrochlorides, showed that the acid of the solution exerted no rearranging action upon the alkamines, nor did the salts of these amines affect the hydrazone precipitation.

It is suggested that this method of analyses is by no means limited to the study of the rearrangement of these two alkalines. Apart from this versatility, the method has the real advantage of throwing the burden of the rate studies upon the formation of the product of rearrangement rather than the disappearance of the rearranging compound.

3. Technique of the Rate Study

a. The course of rearrangement.--The rearrangement of the alkaline hydrochloride was carried out in aqueous solutions of various acidities at 175° and 185°. Each run of a definite concentration of the salt in a definite concentration of hydrochloric acid was made in duplicate, and consisted of a series of 6-8 Carius tubes into each of which had been pipetted 10 cc. of the appropriate solution. Out of a set of sealed tubes immersed in the oil of a thermostat maintained at $175.0^\circ \pm 0.2^\circ$ (or $185.0^\circ \pm 0.2^\circ$) a tube was withdrawn at a recorded interval and cooled rapidly. The contents of the tubes were transferred to 50 cc. Erlenmeyer flasks and the 2,4-dinitrophenylhydrazones of pinacolone precipitated according to the prescribed method. The weights of the collected, dried precipitates were calculated to moles of pinacolone, and correction applied for the 3 per cent pinacolone not isolable through this scheme of precipitation. These corrected values are found in column 3 of the tables.

b. Calculation of results.--The velocity constants were calculated for each concentration of hydrochloric acid from the equation for a reaction of first order or a unimolecular reaction:

$$\begin{aligned} A &\longrightarrow B + C \\ \frac{-d(a-x)}{dt} &= K(a-x) \\ \frac{dx}{dt} &= K(a-x) \\ K &= \frac{1}{t} \ln \frac{a}{(a-x)} \end{aligned}$$

in which a represents the initial concentration of the amino alcohol, and x the amount of amino alcohol reacted.⁶⁴

The values of (x) were assumed equal to the corrected

⁶⁴H. S. Taylor, "Treatise on Physical Chemistry," D. Van Nostrand, New York, 1936, Vol. II, pp. 951, 959.

amount of pinacolone found (M./l.) as given in column 3 of the tables.

The constants, K, calculated for long range intervals of time are given in column 4 of the tables, the factor 4342 is a quotient $\frac{10,000}{2.303}$ used to facilitate the calculation and comparison of these constants with those of Dr. Adams which were reported as K x 4342.

The average K noted in each table was not derived by an arithmetical averaging of the calculated constants,⁶⁵ but by plotting $\log \frac{1}{a-x}$ against time in hours, and determining the slope of the best straight line drawn through these points. This slope multiplied by 2.303 gives the value of K. The best straight lines are drawn with a precision of 3 per cent. The corrected concentrations of pinacolone given in column 5 of the tables were derived from these graphs.

4. Results

a. Rearrangement of 2-aminotetramethylethanol hydrochloride (0.1125 M.) at 175° in 2.08 N. HCl (Table 13).--This run of Dr. Adams was repeated essentially to check the foregoing procedure for the estimation of pinacolone by applying it to a rate study whose constants had already been determined with precision and on a compound very similar to 2-dimethylaminotetramethylethanol hydrochloride. If concordance were obtained in the values of K, such a recheck should prove of further value in that the analyses were made for pinacolone whereas those of Dr. Adams were for the unchanged alkamine.

$$K \text{ (found)} = \frac{321}{4342} = 0.0739$$

$$K \text{ (Dr. Adams)} = \frac{354}{4342} = 0.0815$$

While the difference between these constants is appreciable (10 per cent) and signifies an actual difference of 10 ± 1 per cent between the concentrations of pinacolone directly determined and those calculated from the alkamine concentrations, the difference is not surprising in view of the fact that the methods of analyses were wholly different and for different components of the system.

⁶⁵Roseveare, J. Am. Chem. Soc., 53, 1652 (1931).

The concentrations of pinacolone calculated from the constant of Dr. Adams are (for corresponding times) lower than those actually obtained by direct analyses. This may mean either that precipitation of its 2,4-dinitrophenylhydrazone gives too high a value for the concentration of pinacolone, or that the determination of Dr. Adams gives too high a value for the concentration of alkamine. The alkamine determination (removal of ammonia and subsequent distillation and titration of the alkamine) is more apt to give high values for the alkamine by incomplete removal of ammonia than high values for pinacolone be obtained in a procedure which by the very nature of gravimetric technique tends to give low results. Correction was made, however, for the ammonia in the distillate by Dr. Adams.

b. Rearrangement of 2-dimethylaminotetramethylethanol hydrochloride (0.1125 M.) at 175° (Tables 14-19).--A series of runs at varying concentrations of hydrochloric acid were made and K determined for each concentration of acid. These values are reported in the following table.

TABLE 1

N. HCl.	0.00	0.052	0.208	0.520	1.04	2.08
K	0.0390	0.0671	0.0953	0.202	0.294	0.372

The following conclusions may be drawn from these data:

1) For any one concentration of acid the rate of rearrangement follows the rate mathematically expressed of an intramolecular or first order reaction. Since K increases with increase in acid concentration, C, the rate of rearrangement appears to be that rate peculiar to a pseudo-monomolecular reaction,⁶⁶

$$K_1 = \frac{1}{tC} \ln \frac{a}{a-x}$$

though the relationship between K and acid concentration is not a simple linear one.

2) The rate of rearrangement of 2-aminotetramethylethanol hydrochloride is slower than the corresponding rate of its N-dimethyl derivative. Thus, in neutral aqueous solution at 175°,

⁶⁶Taylor, loc. cit.

$$K_{2\text{-amino}} = \frac{35.4}{4342} = 0.00815$$

$$K_{2\text{-dim.amino}} = \frac{169}{4342} = 0.0390$$

Therefore according to the Stieglitz theory, the rate of deamination being less for the amino compound than for its N-dimethyl derivative, the concentration of rearranging ammonium ion should be greater for the dimethylamino salt and/or the C-N(Me)₂ bond weaker than the C-NH₂ bond. No direct data exist to show quantitatively the influence of either factor, though it seems the effect of concentration upon the actual rate must be very small.

Since 2-aminotetramethylethanol ($K_b = 6.39 \times 10^{-5}$) and 2-phenylaminotetramethylethanol ($K_b = 2.70 \times 10^{-8}$) are each stronger bases than the respective unalkylated amines, ammonia ($K_b = 1.8 \times 10^{-5}$) and aniline ($K_b = 4.6 \times 10^{-10}$), 2-dimethylaminotetramethylethanol should be a slightly stronger base than dimethylamine ($K_b = 7.4 \times 10^{-4}$) and therefore a stronger base than 2-aminotetramethylethanol. If, therefore, the concentrations of unionized ammonium bases in the solutions of both the primary and tertiary amines are calculated and compared, the difference between them, while large, is not significant in view of the predomination of salt in either solution and cannot begin to account for the difference in rates of reaction.

It is evident then that amino compound must rearrange more slowly than its dimethyl derivative because the C-NH₂ bond is stronger than the C-N(Me)₂ bond. No direct evidence has been found on the relative strengths of these bonds. In the free bases the C-N(Me)₂ bond should be the stronger since the additional support given to the C-N linkage by the unshared electrons should be greater. Dimethylamine is a stronger base than ammonia, and it is recognized that the basic character of trivalent nitrogen is a measure of the availability of the unshared electron pair to co-ordinate a proton or other positive ion.⁶⁷ In the salts, however, the electromeric effect will be canceled; and the greater weight of the N-(CH₃)₂ group may weaken its C-N bond sufficiently to account for the difference in rates observed above. Confirma-

⁶⁷J. W. Baker, "Tautomerism," D. Van Nostrand, New York, 1934, p. 22.

tion of the actual difference in strength between the $C-N(CH_3)_2$ and $C-NH_2$ bonds is afforded by comparison of the energies of activation of the rearrangement of the two alkamines: 42,100 and 47,350 cal. respectively. It would be interesting to have parallel studies made on the relative rates of hydrolysis of, say, acetamide and N,N-dimethylacetamide; and a study made on the relative rates of rearrangement of the various alkamines using exhaustive methylation technique.⁶⁸

3) Over a range of acid concentrations the rate of rearrangement of 2-dimethylaminotetramethylethanol hydrochloride appears to be some non-linear function of the acid concentration; the rate of increase falls off with increase in acid concentration but not as rapidly as does that for 2-aminotetramethylethanol hydrochloride.

To interpret these facts it is necessary to postulate that K is the sum of the rates of two concurrent reactions, K_1 and K_2 , where K_1 measures the rate of rearrangement through the amino group and K_2 the rate through the hydroxyl group. This postulation can lead only to a qualitative interpretation of the problem because of our present inadequate knowledge concerning such important factors as the activities of the respective ions, separately and together, at the elevated temperatures and relatively high solution concentrations involved in these studies. If K_1 be assumed equal to the rate of rearrangement of the alkamine hydrochloride in neutral aqueous solution, K_2 may be calculated from the expression,⁶⁹

$$K_2 = K - K_1$$

It is argued, further, that the calculated rate, K_2 , is slower than that experimentally demonstrated for pinacol because of the effect of the positive ammonium group in inhibiting the formation of the oxonium salt. The value of K_2 , both for 2-aminotetramethylethanol hydrochloride and for its N-dimethyl derivative, increases with increasing acid concentrations; but its rate of increase decreases.

It has been shown that K^1 for pinacol, however, is a

⁶⁸Hurd, "The Pyrolysis of Carbon Compounds," Chemical Catalogue Co., New York, 1929.

⁶⁹Adams, *op. cit.*, p. 76.

linear function of the acid concentration. By taking into account a possible salt effect and a series of rough approximations using Bronstead's theory⁷⁰

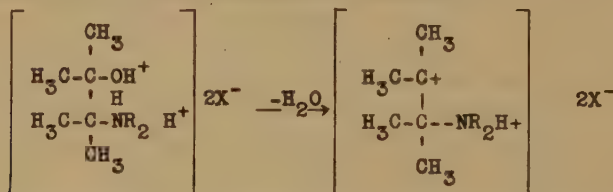
$$v = K_0 C_A C_B 10^{Z_A Z_B \sqrt{u}}$$

it may be demonstrated that the velocity of a bimolecular reaction should be an exponential function of the square root of the ionic strength of the solution in which the reaction is studied. Both K_1 and K^1 must be independent of the ionic strength, since in either case, one of the particles entering into the reaction has zero charge. For pinacol the velocity of rearrangement should be directly proportional to the concentration of the hydrogen ions. For the reaction represented by K_2 , since both Z_A and Z_B are positive and since the function relating K_2 and u is one similar to

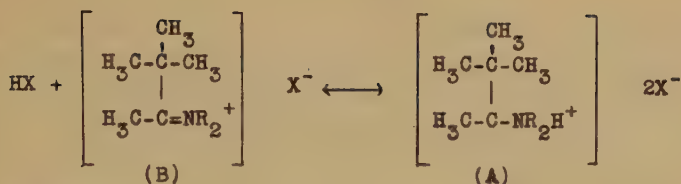
$$\log K_2 = \sqrt{u}$$

where $u = \frac{1}{2} \sum C_i Z_i^2$, the velocity, K_2 , of rearrangement should increase with increase in u ; and in these particular cases of the alkamines, the differences between successive and increasing values of K_2 become progressively greater. But actually, while K_2 does grow numerically larger with u , the differences between successive and increasing values of K_2 become smaller. It is therefore evident that the Bronstead equation does not apply, and that a salt effect cannot explain the increase of K with acid concentrations above equivalency. An interesting attack on this problem might be to attempt the rearrangement of one of these alkamines at constant ionic strength and varying P_H .

K_2 however may represent the rate of at least two reactions. One may postulate that the rearrangement occurs through the oxonium salt of the alkamine as follows:



⁷⁰Bronstead, Chem. Rev., 5, 231 (1928); Adams, op. cit.



where intermediate A, (1) by loss of a proton on the methyl group gives a vinyl derivative, (2) by loss of a proton from the nitrogen atom, a ketimine to which B is related, (3) by the assumption of a hydroxyl group from the environment and the splitting off of an amine, pinacolone or (4) by the direct breaking of the highly unstable linkage $\text{C}^+-\text{NR}_2\text{H}^+$, $-\text{C}^+\ddagger$, which taking up an oxide ion or two hydroxyl ions yields pinacolone.

The production of a vinyl derivative could account readily for the polymeric material associated with these studies at low acid concentration. The formation of a ketimine, while very likely with either the amino or N-phenylaminoethanols, would be difficult to demonstrate because of its instability at these temperatures and concentrations of acid. So far as the mechanism for the rearrangement of 2-dimethylaminotetramethylethanol hydrochloride is concerned, the closely related routes (2) and (4) seem the more probable. An extension of these speculations is not desirable. It is believed that K_2 cannot be a simple measure of rearrangement through the oxonium salt (and therefore a measure of rate of dehydration) but must be a measure of deamination however it occurs.

c. Rearrangement of 2-dimethylaminotetramethylethanol hydrochloride at 185° (Tables 20-23).--

TABLE 2

M.HCl	0.52	0.52	0.52	1.04
M. Alkamine HCl	0.0590	0.900	0.1125	0.1125
K	0.569	0.591	0.588	0.846

These points are of interest:

1) Change in concentration of alkamine hydrochloride with the concentration of added acid constant produces no serious change in K. Average K = 0.583. The maximum deviation is 0.583 - 0.014 or 2.5 per cent. It is questionable that the values for K

can be determined this closely.

While the alkamine concentration in the above series of runs was varied in order to throw further light upon the trend observed in K_v with progress of rearrangement, and K_v does have a lower value with lower concentration of alkamine, no significance can be attached to the correspondence. It so happens the maximum deviation (2.5 per cent) was obtained in this solution in which the greatest error in determination of pinacolone can be expected.

2) Calculation of the temperature coefficient for two different concentrations of hydrochloric acid reveals a surprising concordance:

1.04 N.HCl.

$$K_{175} = 0.294$$

$$K_{185} = 0.810$$

$$\frac{K_{185}}{K_{175}} = 2.87$$

0.52N.HCl

$$K_{175} = 0.202$$

$$K_{185} = 0.583$$

$$\frac{K_{185}}{K_{175}} = 2.88$$

That this is well inside the probabilities of the experiment hardly needs to be pointed out.

3) Calculation of E, the energy of activation:⁷¹

$$\frac{d \ln k}{dt} = \frac{E}{RT^2} \quad (\text{Equation of Arrhenius})$$

$$\log \frac{K_2}{K_1} = \frac{E}{2.303 \times 1.987} \frac{(T_2 - T_1)}{T_2 T_1}$$

2-dimethylaminotetramethylethanol hydrochloride - E - 42,100 cal.

2-phenylaminotetramethylethanol hydrochloride - - E - 35,000 cal.

2-aminotetramethylethanol hydrochloride - - - - E - 47,350 cal.

⁷¹Taylor, op. cit., Vol. II, p. 969.

C. Experimental Details

1. Preparations

a. Pinacol hydrate.--The procedure followed was that described in "Organic Syntheses" save for the larger quantities of materials involved in any single run. Into a 12 l. flask fitted with an adaptor carrying both a large condenser and a separatory funnel was placed 300 g. magnesium turnings and 3,000 cc. dry benzene. To this was slowly added about one-third of a solution of 340 g. mercuric chloride in 1,920 cc. acetone; heat was applied, the remainder of the acetone solution introduced sufficiently rapidly to keep the reaction mixture in vigorous reflux, 950 cc. of acetone in 750 cc. benzene added and the flask contents heated for 5-6 hours. Water was added for hydrolysis and pinacol isolated by the described method, washed with benzene and ligroin and air-dried.⁷²

b. Anhydrous pinacol.--Prepared by the vacuum dehydration of pinacol hexahydrate according to the method of Adams,⁷³ the dry pinacol was subjected to vacuum distillation for final purification. Redistillation served to remove the last trace of water as well as the bulk of the volatile mercury compounds present in pinacol prepared as above, b.p. 90-91° at 15 mm. No further attempt at purification was made since this material served our purpose satisfactorily.

c. Tetramethylethylene chlorohydrin.--The chlorohydrin was obtained by passing a carefully controlled rapid stream of dry gaseous HCl into anhydrous pinacol, rapidly stirred and maintained at a temperature of 40° ± 2°. ⁷⁴ The progress of the reaction was periodically checked by withdrawing a small sample, treating with ice water and observing the behavior of the resulting solid, pressed dry, toward ligroin. Pinacol hexahydrate is insoluble in

⁷²"Organic Syntheses," ed. by Henry Gilman, John Wiley and Sons, Inc., New York, 1932, Coll. vol., p. 448.

⁷³Adams, op. cit., p. 27; Brauer, op. cit., p. 45.

⁷⁴Adams, op. cit., p. 35.

this reagent; the chlorohydrin is soluble. The time consumed for the reaction was usually 4 to 5 hours, seldom more than this. Any extension of this time with the normal rate of HCl passage lowered the yield with the formation of an unknown dark colored highly unstable oil. The chlorohydrin was recovered from the reaction mixture by pouring the straw colored mixture into ice water with rapid agitation, and filtering off the waxy white solid precipitated. A typical run used 59 g. anhydrous pinacol (0.5 mole); from this was obtained 40-48 g. of tetramethylethylene chlorohydrin or a 60-70 per cent yield.

d. 2-dimethylaminotetramethylethanol.--An iron bomb shell similar to that used by Adams⁷⁵ was improvised from a 16 inch length of 2 inch black iron pipe, capped at one end and threaded at the other for fitting of a perforated cap whose 1/4 inch orifice was sealed with a thin copper safety disc. The tube, lined with a removable Pyrex shell, was heated by placing it in a large can and passing steam about it.

A suspension of 50 g. of tetramethylethylene chlorohydrin in 300 g. 27 per cent dimethylamine solution was placed in the Pyrex shell. The bomb was sealed using a commercial pipe-fitter's graphite paste as thread lubricant and binder, heated at 100° for 50 hours, cooled in a salt ice bath, opened; and the liquid contents neutralized with concentrated hydrochloric acid using methyl red as indicator. The aqueous solution of the mixed amine hydrochlorides was then taken down to dryness under reduced pressure. The hydrochlorides were thoroughly dried, powdered, and suspended in 200 to 300 cc. of chilled ether to which with vigorous shaking was slowly added 450-500 g. powdered KOH. The solution was filtered, and the solids washed thoroughly with ether. All filtrates were combined and concentrated by simple distillation. The residue was distilled b.p. 180° (unc.) at 750 mm. Yield 25 g. or 46 per cent of the theory based on the chlorohydrin.

Analysis. Calcd for $C_8H_{19}ON$: C, 66.16 per cent; H, 13.16 per cent; N, 9.65 per cent.
Found: C, 65.12 per cent; H, 12.83 per cent; N, 9.79 per cent.

Redistillation (b.p. 93-94° at 15 mm.) gave a product whose analysis based upon titration against standard acid (methyl red as indicator) was:

⁷⁵Ibid., p. 84.

<u>Sample</u>	<u>H₂SO₄ (0.0968 N.)</u>
0.4256 g. (0.002933 moles)	30.20 cc. (0.002923 moles)
0.3821 g. (0.002633 moles)	27.15 cc. (0.002628 moles)

e. Dimethylaminotetramethylethanol hydrochloride.--The free base was dissolved in dry ether and dry HCl bubbled into the chilled solution until the white crystalline hydrochloride had ceased precipitating. The salt, twice recrystallized by successive solutions in absolute alcohol and reprecipitations with dry ether, washed finally with ether and dried over P₂O₅ in an evacuated dessicator, was distributed between a number of small sealed bottles because of its slightly hygroscopic nature, and stored in this fashion until used, m.p. 194°.

Analysis. Calcd for C₈H₂₀ONCl: Cl, 19.53 per cent.
Found: Cl, 19.47 per cent, 19.44 per cent.

f. 2-aminotetramethylethanol hydrochloride.--This compound was prepared by the method of Adams,⁷⁶ and twice recrystallized from alcohol and ether, m.p. 218°.

Analysis. Calcd for C₆H₁₆ONCl: Cl, 23.07 per cent.
Found: Cl, 22.97 per cent, 22.95 per cent.

g. Pinacolone.--Prepared from pinacol hexahydrate by treatment of the latter with 6 N. H₂SO₄ according to the method of "Organic Syntheses,"⁷⁷ the oil was twice distilled, after careful drying over anhydrous MgSO₄, through an eight ball Snyder column, only the middle cut being taken for each operation, b.p. 106° at 750 mm.

h. Dimethylamine hydrochloride.--The 27 per cent dimethylamine solution of commerce was neutralized with concentrated hydrochloric acid and the resulting solution evaporated to dryness. The salt, repeatedly recrystallized from alcohol and ether and dried over P₂O₅, was kept in a tightly stoppered bottle because of its very hygroscopic nature, m.p. 170°.⁷⁸

2. Methods of Analysis

a. Determination of dimethylamine and 2-dimethylaminotetramethylethanol hydrochlorides.--Either of these hydrochlorides may be determined by liberation of the free base from its salt,

⁷⁶Ibid., p. 84.

⁷⁷"Organic Syntheses," p. 451.

⁷⁸Beilstein, op. cit., Vol. IV, p. 39.

steam distillation of this base into standard acid with subsequent titration of the unconsumed acid against standard alkali. Approximately 0.1 M. solutions of the respective hydrochlorides were made and 10 cc. aliquots of these solutions placed in small Kjeldahl flasks to each of which was added 100 cc. HOH and 2 g. NaOH. The usual technique of the Kjeldahl analysis for determining NH_3 was followed.

TABLE 3

<u>2-dimethylaminotetramethylethanol hydrochloride</u>		
Weight alkamine hydrochloride = 2.0605 g. (0.01135 moles) made up to vol. of 100 cc.		
H_2SO_4 (0.0968N.)	NaOH (0.0984N.)	Amine found
cc.	cc.	moles
25.34	13.42	0.001134
25.06	13.23	0.001126
<u>Dimethylamine hydrochloride</u>		
Weight amine hydrochloride = 1.432 g. (0.01756 moles) made up to vol. of 100 cc.		
27.16	9.00	0.001745
25.06	6.91	0.001747

Several attempts were made to separate the two amines by physical means. Distillation through a column was not at all effective because of the water present. Experiments set up to show that dimethylamine could be separated from the much less volatile alkamine by the bubbling of an inert gas through an alkalized (4 per cent NaOH) solution of the two revealed that even before all the dimethylamine was gone some of the alkamine was lost. The amount of alkamine left in solution in either case was estimated by steam distillation of the blown residue into standard acid and subsequent back titration of the acid with standard alkali. The data are summarized in Table 4.

It was thought then that the nitroso derivative of dimethylamine could be made by treating the aqueous solution of the amines with nitrous acid at such a temperature and such a concentration that the alkamine present in the mixture would be un-

affected. The procedure used for the formation of nitroso-dimethylamine was essentially that used by Taylor and Price in their studies on nitrous acid.⁷⁹ The dimethylamine hydrochloride solution (approx. 0.1 M.) of known concentration was pipetted (10 cc.) into a small Carius tube, its surface was covered with a thin layer of mineral oil and freshly made sodium nitrite solution (10 cc.) added. The tubes were cooled (dry ice-acetone), evacuated, and sealed. At the expiration of the heating time, the tubes were again cooled and opened; and their contents transferred to Kjeldahl flasks and diluted with 100 cc. boiled distilled water. This solution was boiled to remove oxides of nitrogen whereupon an excess of alkali was added with an additional 100 cc. of water and the free amine distilled into standard acid.

Control runs using authentic nitrosodimethylamine⁸⁰ revealed this compound unaffected by the procedure and therefore without effect upon the accuracy of the dimethylamine determinations.

The data are reported in Table 5.⁸¹

TABLE 4

<u>Dimethylamine Hydrochloride</u>			
Weight salt.--1.432 g. (0.01756 moles) made up to vol.--100 cc. N ₂ bubbled 2 hours.			
H ₂ SO ₄ (0.0968 N.) cc. 25.26	NaOH (0.0984 N.) cc. 20.75	Amine Left in Solution	
		moles	per cent
		0.000405	23
<u>Alkamine Hydrochloride</u>			
Weight salt.--1.900 g. (0.01046 moles) made up to vol.--100 cc. N ₂ bubbled 1 hour.			
25.26	15.59	0.000913	88
N ₂ bubbled 2 hours			
25.40	16.56	0.000830	80

⁷⁹Taylor and Price, J. Chem. Soc., 2052 (1929).

⁸⁰Prepared according to method of Renouf, Ber., 13, 2170 (1880).

⁸¹In this and subsequent tables,
R = Me₂C(OH)-CMe₂⁻
mmis. = millimoles

TABLE 5

FORMATION OF NITROSO DIMETHYLAMINE

Effect in change of temperature				
Time = 18 hours				
mmles. $\text{NaNO}_2 = 3.0$				
Variable	Per Cent Nitrosamine Formation	$\text{Me}_2\text{NH}_2\text{Cl}$ mmles.	H_2SO_4 (0.09683 N.) cc.	NaOH (0.09785 N.) cc.
30°	20.6	1.142	26.05	16.56
50°	50.0	1.142	25.09	20.16
	55.0		25.59	20.08
	59.7		25.17	20.23
	84.7	1.214	25.16	22.99
75°-80°	99.7	1.178	25.06	24.64
100°	100		25.06	24.69
Effect in change of reaction time				
Temp. = 100°				
mmles. $\text{NaNO}_2 = 3.0$				
3 hrs.	91.8	1.178	25.80	24.42
	93.7		25.06	23.92
18 hrs.	99.7	1.178	25.06	24.64
	100.0		25.06	24.69
Effect in change of conc. of HNO_2				
Temp. = 75°-80°				
Time = 18 hours				
mmles. HNO_2			H_2SO_4 (0.0968 N.) cc.	NaOH (0.0978 N.) cc.
3.0	84.7	1.214	25.16	22.99
6.0	97.9	1.214	25.17	24.65
Temp. = 100°				
3.0	91.8	1.178	25.80	24.42
	93.7		25.06	23.92
5.0	99.6	1.178	25.11	24.67
	99.0		25.06	24.56

A similar series of blank runs made on the alkamine disclosed that the nitrous acid destroyed 40 per cent of its effective basicity. No pinacolone was discovered using the sensitive

semicarbazone test of Brauer's for its detection.⁸² No pressure was observed on opening the tubes for analyses. The data are reported in Table 6.

TABLE 6

EFFECT OF HNO_2 ON 2-DIMETHYLAMINOTETRAMETHYLETHANOL

$\text{RNMe}_2\text{HCl} = 2.0605 \text{ g. (0.01135 moles 100 cc.)}$			Time = 4 hrs. Temp. = 100° mmls. $\text{NaNO}_2 = 5.0$
H_2SO_4 (0.0968 N.)	NaOH (0.0978 N.)	RNMe_2HCl Unchang. mols.	Per Cent Loss
25.06	16.76	0.000779	38.2
25.14	17.44	0.000719	44.9
25.10	17.43	0.000716	45.2

b. Estimation of pinacolone.--Preliminary experiments indicated the very satisfactory performance of 2,4-dinitrophenylhydrazine, as a reagent for the estimation of pinacolone,⁸³ from acidulated aqueous methanol. A study made of the environment necessary for maximum precipitation of the hydrazone revealed that the chief factors influencing this precipitation were concentration of acid and concentration of methanol in the water of the precipitating medium. The relative concentrations of pinacolone and hydrazine beyond equivalency exerted but a minor effect.

The reagent was prepared by dissolving 2.513 g. 2,4-dinitrophenylhydrazine in 10 cc. concentrated H_2SO_4 in a small Erlenmeyer flask and adding H_3COH slowly until the red color had given way to yellow. Care was taken to avoid excessive warming of the solution. The cool solution was transferred to a 100 cc. volumetric flask⁸⁴ and H_3COH added to volume. Each 10 cc. aliquot of this solution contained 0.00126 moles of the hydrazine or an effective 25 per cent excess over the maximum amount of

⁸²Brauer, op. cit.

⁸³See Ferrante and Blum, Am. J. Pharm., 105, 381-84 (1933).

⁸⁴All volumetric equipment used in this work was carefully calibrated, as were the weights. No inaccuracy greater than 0.2 per cent was permitted.

TABLE 7

DETERMINATION OF PINACOLONE BY PRECIPITATION
OF ITS 2,4-DINITROPHENYLHYDRAZONE

Effect of change in HOH conc. from 25 to 30 vols. per cent Max. no. mmls. (NO ₂) ₂ C ₆ H ₃ N ₂ H ₃ = 1.26				Vol. pptn soln = 40 cc. H ₂ SO ₄ = 1.2 M. mmls. RNMe ₂ HCl = 0.5 mmls. Me ₃ C ₂ MeO = 0.50±0.08		
No.	Per Cent HOH	Per Cent MeOH	Found Per Cent	Me ₃ C ₂ MeO Present mmls.	Found mmls.	Me ₄ C ₂ HN ₂ (NO ₂) ₂ H ₃ C ₆ g.
1	25	68	90.2	0.506	0.457	0.1280
2	25	68	90.8	0.506	0.460	0.1288
3	25	68	90.2	0.458	0.414	0.1158
4	30	63	92.5	0.458	0.424	0.1188
Blank Runs				No Me ₃ C ₂ MeO present.		
5	25	68		No precipitate out of soln.		
6	30	63		Red crystalline precipitate of hydrazine after several hours standing.		

TABLE 8

DETERMINATION OF PINACOLONE BY PRECIPITATION
OF ITS 2,4-DINITROPHENYLHYDRAZONE

Effect of change in HOH conc. from 30 to 50 vols. per cent: 50 per cent HOH added 1 hr. before filtration Max. no. mmls. (NO ₂) ₂ C ₆ H ₃ N ₂ H ₃ = 1.26				Vol. pptn soln = 40 cc. H ₂ SO ₄ = 1.2 M. mmls. RNMe ₂ HCl = 0.05 mmls. Me ₃ C ₂ MeO = 0.50±0.08		
No.	Per Cent HOH	Per Cent MeOH	Found Per Cent	Me ₃ C ₂ MeO Present mmls.	Found mmls.	Me ₄ C ₂ HN ₂ (NO ₂) ₂ H ₃ C ₆ g.
1	35	58	94.2	0.458	0.432	0.1210
2	35	58	94.7	0.586	0.555	0.1555
3	45	46	96.0	0.586	0.562	0.1575
4	45	46	96.2	0.586	0.564	0.1579
5	50	43	97.3	0.554	0.541	0.1516
6	50	43	98.8	0.527	0.521	0.1458
7	56	37	97.2	0.554	0.539	0.1511
8	56	37	96.5	0.586	0.565	0.1584

pinacolone ever determined in these runs. The reagent was made up each day for each series of analyses. No attempt was made at any time to modify the proportions of the components of this solution.

The pinacolone and alkamine-dimethylamine hydrochloride solutions were made by dissolving the appropriate amount of material in 83 per cent aqueous H_3COH and making up to such a volume that a 10 cc. aliquot would contain the desired number of moles of the material. Care was taken in the weighing of materials to avoid loss through volatilization or increase in weight through assumption of water. The actual weights and volumes used are summarized in Table 12 with the key to locate the solution in any specific run.

TABLE 9

DETERMINATION OF PINACOLONE BY PRECIPITATION
OF ITS 2,4-DINITROPHENYLHYDRAZONE

Effect in change of conc. of H_2SO_4 from 1.2 to 2.2 M.	Vol. pptn soln = 40 cc. Per Cent HOH = 25 Per Cent MeOH = 65 mmls. $RNMe_2HCl$ = 0.50 mmls. Me_3C_2MeO = 0.50 ± 0.08
Max. no. mmls. $(NO_2)_2C_6H_3N_2H_3 = 1.26$	

No.	H_2SO_4 M.	Found Per Cent	Me_3C_2MeO Present mmls.	Found mmls.	$Me_4C_2HN_2$ $(NO_2)_2H_3C_6$ g.
1	1.2	90.2	0.458	0.414	0.1158
2	1.6	89.9	0.458	0.412	0.1154
3	2.2	86.6	0.458	0.397	0.1112
				Per Cent HOH = 35	
				Per Cent MeOH = 58	
4	1.2	94.2	0.458	0.432	0.1210
5	1.6	93.9	0.586	0.550	0.1541

Into a 50 cc. Erlenmeyer flask was pipetted 10 cc. of the above solution and to this was added precisely 10 cc. of a solution containing HOH, H_2SO_4 , and H_3COH in proportions designed to give the desired acid and alcohol balance after 10 cc. of the reagent had been added and 10 cc. HOH. All concentrations are calculated on a volume basis which is sufficiently precise for the

TABLE 10

DETERMINATION OF PINACOLONE BY PRECIPITATION
OF ITS 2,4-DINITROPHENYLHYDRAZONE

Effect in change in vol. of soln from 30 to 45 cc.			$H_2SO_4 = 1.6 \text{ M.}$ Per Cent HOH = 34 Per Cent MeOH = 57 mmls. $RNMe_2HCl = 0.50$ mmls. $Me_3C_2MeO = 0.57 \pm 0.02$		
Max. no. mmls. $(NO_2)_2C_6H_3N_2H_3 = 1.26$					
No.	Vol. Soln cc.	Found Per Cent	Me_3C_2MeO Present mmls.	Found mmls.	$Me_3C_2HN_2$ (NO_2) $_2C_6H_3$ g.
1	30	95.2	0.586	0.559	0.1563
2	30	95.6	0.554	0.530	0.1485
3	40	93.9	0.586	0.550	0.1541

TABLE 11

DETERMINATION OF PINACOLONE BY PRECIPITATION
OF ITS 2,4-DINITROPHENYLHYDRAZONE

Effect in change in conc. of Me_3C_2MeO from 0.02 to 0.1 M.			$H_2SO_4 = 1.2 \text{ M.}$ Per Cent HOH = 50 Per Cent MeOH = 43 Vol. soln = 40 cc.			
Max. no. mmls. $(NO_2)_2C_6H_3N_2H_3 = 1.26$						
No.	Present mmls.	Me_3C_2MeO Found Per Cent	Found mmls.	$RNMe_2HCl$ Present mmls.	Me_3NH_2Cl Present mmls.	$Me_3C_2HN_2$ (NO_2) $_2C_6H_3$ g.
1	0.2152	99.2	0.213	0.826	0.154	0.0598
2	0.2152	97.2	0.209	0.826	0.154	0.0586
3	0.4304	98.4	0.424	0.619	0.307	0.1187
4	0.4304	97.7	0.420	0.619	0.307	0.1178
5	0.6456	97.6	0.630	0.413	0.461	0.1766
6	0.6456	97.8	0.631	0.413	0.461	0.1769
7	0.8608	97.7	0.840	0.206	0.614	0.2355
8	0.8608	97.8	0.842	0.206	0.614	0.2358
9	1.076	97.3	1.046	0.000	0.768	0.2932
10	1.076	97.4	1.048	0.000	0.768	0.2935

matter at hand. Because of the fact that with the higher concentrations of water the hydrazine tended to precipitate out, the final percentage determining water was added an hour before filtration. At that time the hydrazine concentration had been reduced to such an extent by hydrazone formation that no precipitation of the former was encountered.

It was demonstrated that this identical method of precipitation would also be effective for the estimation of pinacolone from a mixture obtained on the rearrangement of 2-aminotetra-methylethanol hydrochloride. Neither the ammonium chloride nor alkamine hydrochloride exerted a harmful effect upon the precipitation of the hydrazone, nor did the concentration of acid employed in the precipitation solution rearrange the alkamine. The blank runs revealing this are not reported since they do not differ in any essential respect from those runs here given.

TABLE 12

RNMe_2HCl	$\text{Me}_3\text{C}_2\text{MeO}$	Made to Vol.	Table No.
(a)			
0.9367 g. (5.158 mmls.)	0.2533 g. (2.531 mmls.)	50 cc.	7; 1, 2 9; 1, 2, 3
0.8643 g. (4.759 mmls.)	0.4587 g. (4.582 mmls.)	100 cc.	7; 1, 2, 3, 4 8; 1
0.8207 g. (4.519 mmls.)	0.5864 g. (5.858 mmls.)	100 cc.	8; 2, 3, 4, 8 10; 1, 3
0.8896 g. (4.899 mmls.)	0.5547 g. (5.541 mmls.)	100 cc.	8; 5, 7 10; 2
0.8538 g. (4.702 mmls.)	0.5273 g. (5.268 mmls.)	100 cc.	8; 6
(b)			
2.8117 g. (15.78 mmls.)		150 cc.	11
$\text{Me}_2\text{NH}_2\text{Cl}$			
0.9389 g. (11.52 mmls.)	1.6162 g.	150 cc.	

The solution as set up was allowed to stand 24 hours before filtering. The precipitates were filtered into previously prepared Gooch crucibles (washed, dried, brought to constant weight) with the help of 10 cc. 2 N.H₂SO₄, 10 cc. 20 per cent aqueous H₃COH, followed by 20 cc. HOH. This washing served to remove all traces of excess reagent from the precipitate as well as acid. The crucibles with their precipitates were then dried to constant weight in an oven maintained at 80°. All weighing was done in and out of a CaCl₂ filled desiccator.

The method as developed using as precipitation medium a 43 per cent (by volume) aqueous methanol solution, 1.2 M. with respect to H₂SO₄, was applied to the estimation of pinacolone in the runs on the rearrangement of 2-dimethylaminotetramethylethanol hydrochloride, and of 2-aminotetramethylethanol hydrochloride.

TABLE 13

REARRANGEMENT OF 2-AMINOTETRAMETHYL-
ETHANOL HYDROCHLORIDE

Conc. of added HCl = 2.08 N.		Temp. = 175.0°±0.2°		
Conc. of RNH ₃ Cl = 0.1125 M.				
Time	Me ₄ C ₂ HN ₂ (NO ₂) ₂ H ₃ C ₆ g.	Me ₃ C ₂ MeO		K x 4342
		Found M./L.	Corr. M./L.	
2.03	0.0350	0.0129	0.0130	...
4.00	0.0731	0.0269	0.0265	329
6.00	0.1023	0.0376	0.0383	310
9.00	0.1425	0.0524	0.0531	313
11.00	0.1665	0.0613	0.0612	329
14.00	0.1947	0.0716	0.0714	322
16.00	0.2067	0.0761	0.0770	312
18.00	0.2235	0.0822	0.0818	323
K = 0.0739		Av. dev. = ±1.0 per cent		
= $\frac{321}{4342}$				

3. Apparatus

The thermostat was of 5 gal. capacity, constructed from a steel ether shipping container insulated with 2 in. magnesia pipe

TABLE 14

REARRANGEMENT OF 2-DIMETHYLAMINOTETRA-
METHYLETHANOL HYDROCHLORIDE

Conc. of added HCl = 0.00 N.
 Conc. of RNMe₂HCl = 0.1125 M.

Temp. = 175.0° ± 0.2°

Time	$\text{Me}_4\text{C}_2\text{HN}_2$ $(\text{NO}_2)_2\text{H}_3\text{C}_6$ g.	$\text{Me}_3\text{C}_2\text{MeO}$		K x 4342
		Found M./L.	Corr. M./L.	
1.50	0.0119 (122°)**	0.0044	0.0053*	...
3.50	0.0377 (121°)**	0.0139	0.0133	139
5.50	0.0616	0.0227	0.0207*	201
8.50	0.0983 (111°)**	0.0362	0.0307*	216
11.50	0.1128	0.0415	0.0397	183
19.00	0.1625	0.0598	0.0580	178
26.50	0.1924 (111°)**	0.0708	0.0719	166
5.50	0.0554	0.0204	0.0207	...
11.00	0.1069	0.0393	0.0383	186
16.50	0.1420	0.0523	0.0526	168
22.00	0.1721	0.0633	0.0641	165
26.50	0.1771	0.0652	0.0719*	138
31.00	0.2055	0.0756	0.0778	156
39.50	0.2215	0.0815	0.0881*	135
9.67	0.1044	0.0384	0.0344*	210
17.67	0.1516	0.0558	0.0551	169

$$K = 0.0390 \quad \text{Av. dev.} = \frac{169}{4342} \times 100 = 3.9 \text{ per cent}$$

** It will be noted in Tables 14 and 19, column 2, that the melting points of several of the tared precipitates was taken; m.p. of the authentic 2,4-dinitrophenylhydrazone, 125°. (Allen, J. Am. Chem. Soc., 52, 2955 [1930]). In all runs, particularly toward the end, the precipitates were contaminated with a minute and variable amount of polymeric substance. No ready way was found of avoiding this, and no attempt was made to identify it.

covering held in place with sodium silicate impregnated canvas. This container was securely mounted 8 in. above the floor of a transite protected wooden platform. The space under the container was large enough to hold a 600 watt open grid hot plate. Provision for stirring the fluid of the bath was made by bolting securely to the wall of the can a tubular type suction stirrer. Heavy Stanolind mineral oil (flash point well above 300°) was used for the bath medium. This oil gave service for approximately 200 hours of working time at temperatures of 175°-185° without excessive carbonization and sludge formation. Because of the oil's appreciable vaporization it was found necessary to add oil every twelve hours to maintain working level one inch from the upper edge of the container.

TABLE 15

REARRANGEMENT OF 2-DIMETHYLAMINOTETRA-
METHYLETHANOL HYDROCHLORIDE

Conc. of HCl = 0.052 N.		Temp. = 175.0°±0.2°		
Conc. of RNMe ₂ HCl = 0.1125 M.				
Time	$\text{Me}_4\text{C}_2\text{HN}_2$ $(\text{NO}_2)_2\text{H}_3\text{C}_6$ g.	$\text{Me}_3\text{C}_2\text{MeO}$		K x 4342
		Found M./L.	Corr. M./L.	
4.00	0.0461	0.0170	0.0204*	...
8.00	0.1175	0.0432	0.0436	348
12.00	0.1651	0.0608	0.0599	333
16.00	0.1995	0.0734	0.0723	523
20.00	0.2198	0.0809	0.0817	300
23.50	0.2348	0.0864	0.0881	289
27.00	0.2470	0.0909	0.0932	281
2.00	0.0228	0.0084	0.0095*	...
5.00	0.0755	0.0278	0.0282	299
8.00	0.1210	0.0445	0.0435	308
12.00	0.1625	0.0598	0.0599	296
19.50	0.2245	0.0826	0.0807	310
26.50	0.2482	0.0913	0.0926	282
		K = 0.0671		Av. dev. = ±2.2 per cent
		= 291		
		= 4342		

The sources of heat for this bath were two. The 600 watt hot plate plugged directly into the 110 volt A. C. circuit served to bring the bath temperature up to 160°. A 100 watt light bulb immersed in the bath near the stirrer and connected through a relay and thermo-regulator elevated the temperature and provided the necessary heat control.

The thermo-regulator was of the ordinary mercury in glass type. It was fashioned of Pyrex tubing, the long cylindrical bulb having a capacity of 50-60 cc. and the capillary rising from this having an internal diameter of 1 mm. The metal head supporting the platinum contact needle and its screw adjustment was attached to the glass with litharge-glycerine cement, and the whole head sealed tightly with a removable glass tube whose function was to prevent oil vapors reaching the mercury surface or the capillary walls and fouling contact. The temperature was read from a Bureau of Standards thermometer, and maintained within 0.2°, which was well within the precision demanded by the experiments.

TABLE 16

REARRANGEMENT OF 2-DIMETHYLAMINOTETRA-
METHYLETHANOL HYDROCHLORIDE

Conc. of HCl = 0.208 N. Temp. = 175.0° ± 0.2°
Conc. of RNMe₂HCl = 0.1125 M.

Time	Me ₄ C ₂ HN ₂ (NO ₂) ₂ H ₃ C ₆ g.	Me ₃ C ₂ MeO		K x 4342
		Found M./L.	Corr. M./L.	
1.33	0.0238	0.0088	0.0082*	...
2.67	0.0564	0.0208	0.0218	401
4.00	0.0884	0.0325	0.0338	422
5.33	0.1221	0.0449	0.0441	465
6.67	0.1462	0.0538	0.0532	464
8.00	0.1661	0.0611	0.0609	457
9.33	0.1826	0.0672	0.0677	450
10.67	0.1993	0.0733	0.0736	453
0.50	0.0023	0.0008	0.0000*	...
2.50	0.0527	0.0194	0.0204	396
4.00	0.0798	0.0294	0.0338*	376
8.00	0.1700	0.0626	0.0609	500
12.00	0.2202	0.0810	0.0787	477

K = 0.953

Av. dev. = 2 per cent

= 414

4342

TABLE 17

 REARRANGEMENT OF 2-DIMETHYLAMINOTETRA-
METHYLETHANOL HYDROCHLORIDE

 Conc. of HCl = 0.520 N. Temp. = 175.0° ± 0.2°
 Conc. of RNMe₂HCl = 0.1125 M.

Time	$\text{Me}_4\text{C}_2\text{HN}_2$ $(\text{NO}_2)_2\text{H}_3\text{C}_6$ g.	$\text{Me}_3\text{C}_2\text{MeO}$		K x 4342
		Found M./L.	Corr. M./L.	
1.00	0.0258	0.0095	0.0082*	...
2.00	0.0655	0.0241	0.0272*	822
3.00	0.1149	0.0423	0.0428	833
4.00	0.1553	0.0571	0.0556	898
5.00	0.1847	0.0680	0.0659	911
6.00	0.2019	0.0743	0.0744	862
7.00	0.2236	0.0823	0.0814	888
8.00	0.2379	0.0875	0.0870	878
0.83	0.0175	0.0064	0.0047*	...
1.83	0.0627	0.0231	0.0244	744
2.83	0.1081	0.0398	0.0403	821
3.83	0.1511	0.0556	0.0536	902
5.33	0.1877	0.0691	0.0689	863
7.83	0.2280	0.0839	0.0862	814

K = 0.202

Av. dev. = ±2.2 per cent

$$= \frac{877}{4342}$$

A large basket of 16 compartments improvised from metal lath, and so slung above the bath that it could be raised and lowered into the oil, allowed for simultaneous immersion of the bomb tubes. The tubes themselves consisted of cylindrical glass bulbs of 20 cc. capacity and 16 mm. inside diameter tapering to a neck fashioned of 10 mm. Pyrex tubing.

4. Technique of the Rate Study

The requisite amount of dimethylaminotetramethylethanol hydrochloride was weighed out directly into a tared volumetric flask whose capacity was 100 cc. The proper number of cc. of 2.080 N. HCl were pipetted in to render the solution in the flask

TABLE 18

REARRANGEMENT OF 2-DIMETHYLAMINOTETRA-
METHYLETHANOL HYDROCHLORIDE

Conc. of HCl = 1.04 N.
 Conc. of RNMe₂HCl = 0.1125 M. Temp. = 175.0° ± 0.2°

Time	$\text{Me}_4\text{C}_2\text{HN}_2$ $(\text{NO}_2)_2\text{H}_3\text{C}_6$ g.	$\text{Me}_3\text{C}_2\text{MeO}$		K x 4342
		Found M./L.	Corr. M./L.	
0.67	0.0218	0.0080	0.0065*	...
1.33	0.0611	0.0225	0.0254*	973
2.00	0.1168	0.0430	0.0408	1330
2.67	0.1487	0.0547	0.0538	1290
3.33	0.1735	0.0638	0.0641	1240
4.00	0.1972	0.0726	0.0727	1260
4.67	0.2155	0.0793	0.0797	1280
5.33	0.2302	0.0847	0.0855	1230
0.75	0.0285	0.0105	0.0093*	
1.42	0.0727	0.0268	0.0295*	1130
2.09	0.1169	0.0430	0.0429	1250
2.75	0.1511	0.0556	0.0552	1270
3.42	0.1787	0.0658	0.0654	1270
4.09	0.2027	0.0746	0.0737	1290
4.75	0.2242	0.0825	0.0810	1330

$$K = 0.294$$

$$\text{Av. dev.} = \pm 2.2 \text{ per cent}$$

$$= \frac{1276}{4342}$$

the required normality in acid when diluted with boiled distilled water to the graduation. Into each of the bomb tubes were pipetted 10 cc. aliquots of this solution; the tube contents were frozen and the tubes sealed.

The tubes were warmed by simultaneous immersion in an oil bath maintained at 100°, and after 5 min. in this bath were transferred at once to the operating thermostat. The time of immersion was noted. A tube was removed after a noted time, so designated, cooled at 100° for 2 min. and stored in an ice bath. Usually one complete run was made before the tubes were opened for analysis.

The tip of the tube was broken, then the neck itself at a point about 5 cm. from the bulb. Care was taken to avoid con-

TABLE 19

 REARRANGEMENT OF 2-DIMETHYLAMINOTETRA-
METHYLETHANOL HYDROCHLORIDE

Conc. of HCl = 2.08 N.		Temp. = 175.0°±0.2°		
Conc. of RNMe ₂ HCl = 0.1125 M.				
Time	$\text{Me}_4\text{C}_2\text{HN}_2$ $(\text{NO}_2)_2\text{H}_3\text{C}_6$ g.	Me ₃ C ₂ MeO		K x 4342
		Found M./L.	Corr. M./L.	
0.50	0.0216	0.00795	0.0091*	
1.00	0.0714 (123°)	0.0263	0.0266	1672
1.50	0.1121	0.0413	0.0412	1666
2.00	0.1467	0.0540	0.0534	1680
2.50	0.1709	0.0629	0.0634	1618
3.00	0.1900	0.0699	0.0716	1559
3.30	0.2059	0.0758	0.0785	1515
0.30	0.0043	0.0016	0.0011*	
0.63	0.0340 (121°)	0.0125	0.0140*	1380
0.97	0.0703	0.0259	0.0256	1610
1.47	0.1135	0.0418	0.0404	1675
2.47	0.1668	0.0614	0.0616	1553
3.97	0.2152 (120°)	0.0792	0.0771	1425
K = 0.372		Av. dev. = ±2.0 per cent		
= $\frac{1615}{4342}$				

tamination of the solution with splinters of broken glass as the volume demands for successful 2,4-dinitrophenylhydrazone precipitation precluded possibility of filtration and consequent thorough washing of the filtration medium whether porous plate or paper. The contents of the tube were poured into a 50 cc. Erlenmeyer flask quickly, and the walls of the tube rinsed down carefully three times with a total of 10 cc. of acidulated H₃COH solution (17 cc. H₂SO₄ diluted to 100 cc. with H₃COH). The flask was stoppered. The contents of the other tubes were transferred in like manner. Then into each of the flasks was pipetted 10 cc. of the 2,4-dinitrophenylhydrazine reagent, and each flask re-

stoppered. The flasks were shaken and left undisturbed for 24 hours.

The rate of appearance of the hydrazone seemed to be determined wholly by and in direct proportion to the amount of pinacolone present. It is conceivable that this could be made a method of analysis for pinacolone in low concentrations if scrupulous attention to detail were observed throughout.

5. Rearrangement of 2-Aminotetramethylethanol hydrochloride

A run made by Dr. Adams⁸⁵ on 2-aminotetramethylethanol hydrochloride was repeated at 175° on a 0.1125 M. solution of the alkamine hydrochloride, 2.08 N. with respect to HCl.

TABLE 20

REARRANGEMENT OF 2-DIMETHYLAMINOTETRAMETHYLETHANOL HYDROCHLORIDE

Conc. of HCl = 0.52 N. Temp. = 185.0° ± 0.2°
 Conc. of RNMe₂HCl = 0.0590 M.

Time	$\text{Me}_4\text{C}_2\text{HN}_2$ $(\text{NO}_2)_2\text{H}_3\text{C}_6$ g.	$\text{Me}_3\text{C}_2\text{MeO}$		K x 4342
		Found M./L.	Corr. M./L.	
0.33	0.0094	0.0035	0.0028*	
0.67	0.0305	0.0112	0.0126*	1950
1.00	0.0553	0.0204	0.0206	2380
1.33	0.0732	0.0269	0.0273	2380
1.67	0.0891	0.0328	0.0328	2450
2.00	0.0927	0.0341	0.0373*	2090
2.33	0.1110	0.0408	0.0410	2420
2.67	0.1153	0.0424	0.0441	2250

K = 0.569

Av. dev. = ± 1.6 per cent

$$= \frac{2471}{4342}$$

The data were obtained along the methods outlined above and are summarized in Table 13; columns 1 and 2.

⁸⁵Adams, op. cit., p. 103, Table 48.

TABLE 21

REARRANGEMENT OF 2-DIMETHYLAMINOTETRA-
METHYLETHANOL HYDROCHLORIDE

Conc. of HCl = 0.52 N.

Conc. of RNMe₂HCl = 0.0900 M.

Temp. = 185.0° ± 0.2°

Time	Me ₄ C ₂ HN ₂ (Me ₂) ₂ HC ₂ g.	Me ₃ C ₂ MeC		K x 4342
		Found M./L.	Calc. M./L.	
0.33	0.0176	0.0065	0.0042	
0.67	0.0504	0.0165	0.0195	2070
1.00	0.0856	0.0319	0.0321	2370
1.33	0.1163	0.0428	0.0425	2480
1.67	0.1357	0.0499	0.0510	2390
2.00	0.1619	0.0596	0.0580	2630
2.33	0.1746	0.0643	0.0637	2560
2.67	0.1854	0.0682	0.0683	2500

K = 0.592

Av. dev. = 11.5 per cent

= $\frac{2565}{4342}$

TABLE 22

REARRANGEMENT OF 2-DIMETHYLAMINOTETRA-
METHYLETHANOL HYDROCHLORIDE

Conc. of HCl = 0.52 N.

Conc. of RNMe₂HCl = 0.1125 M.

Temp. = 185.0° ± 0.2°

Time	Me ₄ C ₂ HN ₂ (Me ₂) ₂ HC ₂ g.	Me ₃ C ₂ MeC		K x 4342
		Found M./L.	Calc. M./L.	
0.33	0.0180	0.0066	0.0000*	1350
0.67	0.0453	0.0170	0.0171	1960
1.00	0.0936	0.0341	0.0341	1920
1.33	0.1188	0.0445	0.0431*	2450
1.67	0.1699	0.0625	0.0598	2370
2.00	0.1995	0.0696	0.0629	2200
2.33	0.2012	0.0740	0.0767	2360
2.67	0.2243	0.0827	0.0830	

K = 0.568

Av. dev. = 12.6 per cent

= $\frac{2653}{4342}$

TABLE 23

 REARRANGEMENT OF 2-DIMETHYLAMINOTETRA-
METHYLETHANOL HYDROCHLORIDE

Conc. of HCl = 1.04 N.		Temp. = 185.0°±0.2°		
Conc. of RNMe ₂ HCl = 0.1125 M.				
Time	Me ₄ C ₂ HN ₂ (NO ₂) ₂ H ₃ C ₆ g.	Me ₃ C ₂ MeO		K x 4342
		Found M./L.	Corr. M./L.	
0.17	0.0049	0.0018	0.0000 [*]	
0.30	0.0292	0.0107	0.0097 [*]	2180
0.47	0.0632	0.0233	0.0232	3130
0.63	0.0931	0.0343	0.0349	3240
0.83	0.1278	0.0470	0.0470	3600
1.00	0.1520	0.0559	0.0556	3500
1.17	0.1744	0.0642	0.0631	3600
1.33	0.1936	0.0712	0.0696	3660

$$K = 0.846$$

$$\text{Av. dev.} = \pm 1.2 \text{ per cent}$$

$$= \frac{3673}{4342}$$

 6. Rearrangement of 2-Dimethylaminoethylethanol Hydrochloride

a. Rearrangement at 100°.--Three Carius tubes were set up, each containing 1.8 g. of the aminoalcohol. Into each of the tubes was placed 10 cc. 1 N., 4 N., and 6 N. HCl respectively. These tubes were then sealed and heated by steam for 10 hours. From them no pinacolone was isolable, either by sensitive semicarbazone test as developed by Brauer (desiccator method)⁸⁶ or by application of the 2,4-dinitrophenylhydrazones precipitation method described in these pages.

b. Rearrangement at 180°.--Preliminary qualitative tests indicated the rearrangement occurred at this temperature in 2 N. HCl. Therefore a Carius tube containing 0.1734 g. (0.955 mmls.) of the alkamine hydrochloride dissolved in 10 cc. 2 N. HCl was heated for 3 hours.

Using 2,4-dinitrophenylhydrazine as reagent, an analysis was made for pinacolone. Found: 0.252 g. (0.901 mmls.) of the 2,4-dinitrophenylhydrazones of pinacolone, or a yield of 93.6 per

⁸⁶Brauer, op. cit.

cent.

c. Rearrangement at 175°.--The concentration of the alkamine hydrochloride was held at 0.1125 M. One run was made on the pure hydrochloride with no added aqueous acid. Five runs were made in which the acid concentration was varied from 0.052 N. to 2.08 N. All runs were carried out in duplicate. The duplicate determination was made at a different time and with a sample of the alkamine from a different preparation. For each run 5 to 8 tubes were filled. The data derived are summarized in Tables 14 to 19 inclusive; columns 1 and 2.

d. Rearrangement at 185°.--For three runs the alkamine salt concentration was varied from 0.0590 M. to 0.1125 M. with the HCl concentration maintained at 0.52 N. The fourth run was made with the concentration of alkamine salt at 0.1125 M. and the HCl concentration at 1.04 N. The results of these runs are summarized in Tables 20 to 23 inclusive; columns 1 and 2.

D. Summary

1. A brief survey of the literature has been presented.
2. The mechanism offered by Dr. Stieglitz for the pinacol and alkamine rearrangements has been reviewed, and slightly amended.
3. An improved analysis for pinacolone in rearrangement mixture has been developed using 2,4-dinitrophenylhydrazine as precipitating agent. It has been demonstrated that with this hydrazone and by ordinary gravimetric technique pinacolone may be estimated to an accuracy of 97 per cent and precision of 0.5 per cent.
4. The rate of rearrangement of 2-aminotetramethylethanol hydrochloride (0.1125 M.) in 2.08 N. aqueous hydrochloric acid, which was determined by Dr. Adams, has been checked.
5. It has been demonstrated that 2-dimethylaminotetramethylethanol hydrochloride rearranges in aqueous solution to pinacolone and dimethylamine hydrochloride.
6. This alkamine hydrochloride (0.1125 M.) has been rearranged in aqueous hydrochloric acid whose concentrations ranged from 0.052 N. to 2.08 N. at 175°; and the rates of rearrangement of the alkamine at these concentrations determined.
7. From this set of data obtained at 175° and from a similar set obtained at 185°, the temperature coefficient of the reaction has been calculated.
8. It has been shown that 2-dimethylaminotetramethylethanol hydrochloride at the same concentration and at the same concentrations of acid rearranges at a faster rate than 2-aminotetramethylethanol hydrochloride. An explanation for this has been offered.
9. The rate of rearrangement of 2-dimethylaminotetramethylethanol hydrochloride in aqueous acid appears to be that of an intramolecular or first order reaction. The rate of rearrangement is some non-linear function of the acid concentration. This function is a different function than that found by Dr. Adams for the rearrangement of 2-aminotetramethylethanol hydrochloride in

aqueous acid. An explanation is offered for these facts, and the data interpreted on the basis of the Stieglitz theory.

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